

WEST Search History

DATE: Monday, March 17, 2003

<u>Set Name</u> side by side	<u>Query</u>	<u>Hit Count</u>	<u>Set Name</u> result set
<i>DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=OR</i>			
L5	L4 and Cyr61	5	L5
L4	Lau-L\$.in.	187	L4
<i>DB=USPT; PLUR=YES; OP=OR</i>			
L3	cyr61 same (mitogen or growth or chemoat\$)	17	L3
<i>DB=USPT,JPAB,EPAB,DWPI; PLUR=YES; OP=OR</i>			
L2	Cyr61.ab. or Cyr61.clm.	7	L2
<i>DB=PGPB; PLUR=YES; OP=OR</i>			
L1	Cyr61.ab. OR Cyr61.clm.	2	L1

END OF SEARCH HISTORY

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NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2	Apr 08	"Ask CAS" for self-help around the clock
NEWS	3	Apr 09	BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS	4	Apr 09	ZDB will be removed from STN
NEWS	5	Apr 19	US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS	6	Apr 22	Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS	7	Apr 22	BIOSIS Gene Names now available in TOXCENTER
NEWS	8	Apr 22	Federal Research in Progress (FEDRIP) now available
NEWS	9	Jun 03	New e-mail delivery for search results now available
NEWS	10	Jun 10	MEDLINE Reload
NEWS	11	Jun 10	PCTFULL has been reloaded
NEWS	12	Jul 02	FOREGE no longer contains STANDARDS file segment
NEWS	13	Jul 22	USAN to be reloaded July 28, 2002; saved answer sets no longer valid
NEWS	14	Jul 29	Enhanced polymer searching in REGISTRY
NEWS	15	Jul 30	NETFIRST to be removed from STN
NEWS	16	Aug 08	CANCERLIT reload
NEWS	17	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS	18	Aug 08	NTIS has been reloaded and enhanced
NEWS	19	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS	20	Aug 19	IFIPAT, IFICDB, and IFIUDB have been reloaded
NEWS	21	Aug 19	The MEDLINE file segment of TOXCENTER has been reloaded
NEWS	22	Aug 26	Sequence searching in REGISTRY enhanced
NEWS	23	Sep 03	JAPIO has been reloaded and enhanced
NEWS	24	Sep 16	Experimental properties added to the REGISTRY file
NEWS	25	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS	26	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS	27	Oct 21	EVENTLINE has been reloaded
NEWS	28	Oct 24	BEILSTEIN adds new search fields
NEWS	29	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS	30	Oct 25	MEDLINE SDI run of October 8, 2002
NEWS	31	Nov 18	DKILIT has been renamed APOLLIT
NEWS	32	Nov 25	More calculated properties added to REGISTRY
NEWS	33	Dec 02	TIBKAT will be removed from STN
NEWS	34	Dec 04	CSA files on STN
NEWS	35	Dec 17	PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS	36	Dec 17	TOXCENTER enhanced with additional content
NEWS	37	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS	38	Dec 30	ISMEC no longer available
NEWS	39	Jan 13	Indexing added to some pre-1967 records in CA/CAPLUS
NEWS	40	Jan 21	NUTRACEUT offering one free connect hour in February 2003
NEWS	41	Jan 21	PHARMAML offering one free connect hour in February 2003
NEWS	42	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS	43	Feb 13	CANCERLIT is no longer being updated
NEWS	44	Feb 24	METADEX enhancements
NEWS	45	Feb 24	PCTGEN now available on STN
NEWS	46	Feb 24	TEMA now available on STN

NEWS 47 Feb 26 NTIS now allows simultaneous left and right truncation
NEWS 48 Feb 26 PCTFULL now contains images
NEWS 49 Mar 04 SDI PACKAGE for monthly delivery of multifile SDI results

NEWS EXPRESS January 6 CURRENT WINDOWS VERSION IS V6.01a,
CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002
NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS INTER General Internet Information
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NEWS PHONE Direct Dial and Telecommunication Network Access to STN
NEWS WWW CAS World Wide Web Site (general information)

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* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 10:51:28 ON 17 MAR 2003

=> file pctfull
COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
0.84	0.84

FULL ESTIMATED COST

FILE 'PCTFULL' ENTERED AT 10:53:33 ON 17 MAR 2003
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FILE LAST UPDATED: 13 MAR 2003 <20030313/UP>
MOST RECENT UPDATE WEEK: 200309 <200309/EW>
FILE COVERS 1978 TO DATE

<<< GRAPHIC IMAGES NOW AVAILABLE --> SEE NEWS >>>

=> s Cyr61
L1 32 CYR61

=> s l1 and py<=1997
309062 PY<=1997
L2 1 L1 AND PY<=1997

=> d ibib abs kwic l2

L2 ANSWER 1 OF 1 PCTFULL COPYRIGHT 2003 Univentio
ACCESSION NUMBER: 1997033995 PCTFULL ED 20020514
TITLE (ENGLISH): EXTRACELLULAR MATRIX SIGNALLING MOLECULES
TITLE (FRENCH): MOLECULES DE SIGNALISATION DE MATRICE EXTRACELLULAIRE
INVENTOR(S): LAU, Lester, F.
PATENT ASSIGNEE(S): MUNIN CORPORATION;
LAU, Lester, F.
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE

WO 9733995	A2	19970918

DESIGNATED STATES

W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI
GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD
MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SK TJ
TM TR TT UA UG US UZ VN GH KE LS MW SD SZ UG AM AZ BY
KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT
LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD
TG

APPLICATION INFO.: WO 1997-US4193 A 19970314

PRIORITY INFO.: US 1996-60/013,958 19960315

ABEN Polynucleotides encoding mammalian ECM signalling molecules affecting the cell adhesion, migration, and proliferation activities characterizing such complex biological processes as angiogenesis, chondrogenesis, and oncogenesis, are provided. The polynucleotide compositions include DNAs and RNAs comprising part, or all, of an ECM signalling molecule coding sequence, or biological equivalents. Polypeptide compositions are also provided. The polypeptide compositions comprise mammalian ECM signalling molecules, peptide fragments, inhibitory peptides capable of interacting with receptors for ECM signalling molecules, and antibody products recognizing **Cyr61**. Also provided are methods for producing mammalian ECM signalling molecules. Further provided are methods for using mammalian ECM signalling molecules to screen for, and/or modulate, disorders associated with angiogenesis, chondrogenesis, and oncogenesis; ex vivo methods for using mammalian ECM signalling molecules to prepare blood products are also provided.

ABFR L'invention porte sur des polynucleotides codant des molecules de signalisation ECM de mammiferes influant sur les activites d'adhesion, de migration, et de proliferation caracteristiques de processus biologiques complexes tels que l'angiogenese, la condrogenese, et l'oncogenese. Les compositions de polynucleotides comportent des ADN et des ARN comprenant en partie ou en totalite une sequence codant une molecule de signalisation ECM ou des equivalents biologiques. L'invention porte egalement sur des compositions de polypeptides. Lesdites compositions de polypeptides comprenant des molecules de signalisation de matrices extracellulaires de mammiferes, des fragments de peptides, des peptides inhibiteurs capables d'interagir avec les recepteurs des molecules de signalisation de matrices extracellulaires, et des anticorps reconnaissant la proteine **Cyr61**. L'invention porte en outre sur des procedes de production de molecules de signalisation de matrices extracellulaires; sur des procedes d'utilisation desdites molecules pour depister et/ou traiter differents troubles lies a l'angiogenese, la condrogenese, et l'oncogenese, et sur des procedes ex vivo d'utilisation desdites molecules pour la preparation de produits sanguins.

PI WO 9733995 A2 19970918

ABEN . . . ECM signalling molecules, peptide fragments, inhibitory peptides capable of interacting with receptors for ECM signalling molecules, and antibody products recognizing **Cyr61**. Also provided are methods for producing mammalian ECM signalling molecules. Further provided are methods for using mammalian ECM signalling molecules. . .

ABFR . . . peptides inhibiteurs capables d'interagir avec les recepteurs des molecules de signalisation de matrices extracellulaires, et des anticorps reconnaissant la proteine **Cyr61**. L'invention porte en outre sur des procedes de production de molecules de signalisation de matrices extracellulaires; sur des procedes d'utilisation. . .

DETD - 19 -

DETAILED DESCRIPTION OF THE INVENTION

In the mouse, the **Cyr61** protein has been found to influence cell adhesion, migration, and proliferation. The **cyr61** gene, which encodes

Cyr61, is an immediate-early gene that. . .

.
In urine **Cyr61** is set out in SEQ ID NO:2. (The human **Cyr61** amino acid sequence is presented in SEQ ID NO:4). **Cyr61** is a 41 kDa

polypeptide exhibiting 39 cysteine residues, approximately 10% of the 379

amino acids constituting the unprocessed protein. Yang et. . .

.
in SEQ ID NO: 1. The degeneracies occur in positions

- 23 -

complementary to the third positions of codons in mouse **cyr61** as set forth in

SEQ ID NO: 1. The amplified **cyr61** cDNA was cloned into the pBlueScript SK + vector (Stratagene, La. . .

.
al. ,

Geisler 60:65-74 (1987). These fusion constructs were generated using standard

techniques, as described below in the context of a phosphoglycerokinase promoter (pgk-1)-**cyr61** fusion. An XhoI-ScaI genomic DNA fragment

containing the entire **cyr61** coding region and all introns, but lacking the transcription initiation site and. . .

.
the

metabolic fate of the expressed proteins. Members of the cysteine-rich protein

I 0 family have been localized. As discussed above, secreted

Cyr61 is found in

the ECM and on the cell surface but not in the culture medium (Yang and Lau, 1991), yet secreted. . .

.
This purification procedure was repeated at least five times with similar results. The typical yield was 3-4 mg of 90% pure **Cyr61** protein from 500 ml of conditioned medium.

.
each protein is devoid of cysteines. See, O'Brien et al., Cell Growth & Diff. 3:645-654 (1992). A cysteine-free region in the InUrine **Cyr61** amino acid sequence is found between amino acid residues 164 to 226

(SEQ ID NO:2). A corresponding cysteine-free region is found. . . human

Cyr61 amino acid sequence between amino acid residues 163 to 229 (SEQ ID NO: 4). More particularly, the mouse and human **Cyr61** proteins are most

divergent between **Cyr61** amino acids 170-185 and 210 Other members of the ECM signalling molecule family of cysteine-rich proteins',. . .

003 integrin, or vitronectin receptor. The α_3 integrin, in association with other integrins, forms protein clusters providing focal points for cytoskeletal attachment.

Cyr61 induces the formation of protein clusters, including the protein clusters containing the α_3 integrin. In addition, using an in vitro assay, the biological effects of **Cyr61**, including **Cyr61** -induced cell adhesion and mitogenesis, were abolished by the addition of either one of two monoclonal antibodies- LM609 (Cheresh, Proc.

cell adhesion properties of **Cyr61** were used to identify the receptor, which is a divalent cation-sensitive cell surface receptor. The ability of **Cyr61** to mediate cell adhesion, coupled with the strict requirement for divalent cations in the process, indicated that **Cyr61** interacts with one of.

tissue culture supernatants are removed from wells containing growing hybridomas, and tested for the presence of anti-**Cyr61** antibodies by binding to recombinant human **Cyr61** bound to nitrocellulose and screening with labeled and-
immunoglobulin antibody in a standard antibody-capture assay. Cells from positive wells are grown and. . . The cloned cell lines are stored frozen. Monoclonal antibodies are collected and purified using standard techniques, e.g., hydroxylapatite chromatography. In an alternative, **Cyr61** peptides used as antigens, may be attached to immunogenic carriers such as keyhole limpet hemocyanin carrier protein, to elicit monoclonal anti-**Cyr61** antibodies.

a wide variety of polypeptides, well known to those of skill in the art, may be used in the formation of **Cyr61** fusion polypeptides according to the invention.

amino acid sequence that is conserved between murine **Cyr61** (SEQ ID NO:2) and human **Cyr61** (SEQ ID NO:4) competes with native **Cyr61** for its binding sites. This competition thereby inhibits the action of native **Cyr61**.

invention, inhibitory peptides were designed to compete with **Cyr61**. These inhibitory peptides, like the antibodies of the preceding Example, exemplify modulators of **Cyr61** activity, as described in the context of a variety of assays for **Cyr61** activity that are disclosed herein. The peptide design was. . . (SEQ ID NO:17) of SEQ ID NO:2, have been synthesized. A comparison of the murine **Cyr61** amino acid sequence and the human **Cyr61** amino acid sequence reveals that similar domains from the human protein may be used in the design of peptides inhibiting human.

also attach internally to the cytoskeleton. Therefore, murine Cyr61, and human Cyr61 (see below), are, in part, adhesion molecules, a characteristic distinguishing Cyr61 from conventional growth factors. Those of skill in the art will also recognize that the $\alpha_5\beta_1$ integrin can be used, in conjunction with Cyr61, to screen for modulators of Cyr61 binding to its receptor. In one embodiment, the integrin is immobilized and exposed to either (a) Cyr61 and a suspected modulator of receptor binding; or (b) Cyr61 alone. Subsequently, bound Cyr61 is detected, e.g., by anti-Cyr61 antibody that is labeled using techniques known in the art, such as radiolabelling, fluorescent labelling, or the like. The binding of Cyr61 to its receptor would increase binding of Cyr61. (and an inhibitor would decrease Cyr61), relative to the binding by Cyr61 alone.

Polystyrene Petri dishes were coated with 2 μ l of a 10 μ g/ml solution of

Cyr61 or fibronectin in PBS with 0.1% BSA and treated as described above.

10^4 cells and was incubated for 2 hours. Cell spreading was analyzed by microscopy at 100-fold magnification. The results indicate that murine Cyr61 induces HUVE cell spreading to approximately the same extent as fibronectin. The efficient attachment (see above) and spreading of cells on murine Cyr61-coated substrates indicated that Cyr61 may interact with a signal-transducing cell surface receptor, leading to a cascade of cytoskeletal rearrangements and possible formation of focal contacts. Consequently, Cyr61 and Cyr61-related polypeptides may prove useful in controlling cell adhesion, e.g., the cell adhesion events that accompany metastasizing cancer cells, organ.

spreading was examined on cells plated on 96 well polystyrene petri dishes coated with 2.5 μ l of a 20 μ g/ml solution of Cyr61, Fisp12 or fibronectin. 10^4 cells were plated on each dish and cell spreading was analyzed 90 min. after plating by microscopy.

In an alternative embodiment, a suspected modulator of angiogenesis is combined with Cyr61 and the combination is added before, or after, formation of a gel. In this embodiment, a control is established by the use of a Cyr61.

by first removing a 2-cm diameter central core of sponge. PBS or an RGDS peptide (other possible test compounds include fragments of

Cyr61, RGDS

peptide, small molecules such as i-nannose phosphate) at 1 00 AM were added to the sponge core which was then coated.

cell

migration are determined. A promoter of **Cyr61** activity will increase the rate

of cell iniation relative to cell migration induced by **Cyr61**

alone; an

6

inhibitor will decrease the rate of cell migration relative to the level ascribable to **Cyr61** alone.

1) no supplementation, 2) inurine **Cyr61**; 3) bFGF; 4) murine **Cyr61** and

bFGF; 5) PDGF-BB; and 6) murine **Cyr61** and PDGF. After 18-20 hours of incubation, cells were washed with PBS and fixed.

Logarithmically grown mink lung epithelial cells (MVIILI, CCL64) were treated with various concentrations of TGF-01 (Gibco-BRL) and 2 Ag/ml of **Cyr61** or FispI2 for 18 hours; [³H]-thymidine was then added to

I A011111 for

2 hours. Thynidine incorporation was deten-nined as described.

It is known that TGF-O acts

to inhibit DNA synthesis in epithelia] cells (Satterwhite et al., 1994).

It was

observed that both **Cyr61** and FispI2 enhanced the ability of

TGF-O to inhibit

DNA synthesis in inink lung epithelia] cells. The data demonstrate that both

recombinant.

cornea assay for modulators of angiogenesis. For example, in one embodiment of the invention, dose of an angiogenic factor such as

Cyr61

could be used in cornea assays for positive effectors of the angiogenic activity

of **Cyr61**. An appropriate dose of Cyi-61 would initially be determined by titration of the dose response relationship of **Cyr61** with angiogenic events.

Therefore, the ability of **Cyr61** to promote differentiation of mesenchymal

cells plated at densities above and below the threshold for

chondrogenesis was

assessed. Cells plated at 2.5.

However, when **Cyr61** was added, these sub-threshold density cultures fon-ned

nodules and incorporated Sulfate to a level similar to that in cultures plated at

3 x 10⁴ cells/ml, which supports chondrogenesis. Therefore,

Cyr61 can

promote chondrogenesis in mesenchymal cells plated at non-chondrogenic, sub-threshold densities.

resulted in a

2-fold enhancement in [³⁵S]-sulfate incorporation in cultures plated at densities

ranging from 3 to 10 x 10⁴ cell/ml. Therefore, **Cyr61** can

further enhance

chondrogenesis in high density micromass cultures, which have apparently

not
reached a maximal degree of differentiation.

invention. Using either approach, the
DNA is then subjected to analysis. One analytical approach involves
nucleotide sequence determination of particular regions of **CYr61**
or of the
entire gene. The available human c-vr61 coding sequence, presented in
SEQ
ID NO:3 herein, facilitates the design of sequencing. . . .

CLMEN 21 The method according to claim 19 wherein said human **Cyr61**
-specific
bioniolecule is an anti-human Cyr61 antibody.

=> file .gary
COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
5.25	6.09

FULL ESTIMATED COST

FILE 'MEDLINE' ENTERED AT 10:56:24 ON 17 MAR 2003

FILE 'CANCERLIT' ENTERED AT 10:56:24 ON 17 MAR 2003

FILE 'BIOSIS' ENTERED AT 10:56:24 ON 17 MAR 2003
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FILE 'SCISEARCH' ENTERED AT 10:56:24 ON 17 MAR 2003
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=> s Cyr61
L3 514 CYR61

=> s l3 and py<=1997
2 FILES SEARCHED...
3 FILES SEARCHED...
L4 76 L3 AND PY<=1997

=> s l3 and py<=1996
2 FILES SEARCHED...
3 FILES SEARCHED...
L5 47 L3 AND PY<=1996

=> dup rem l5
PROCESSING COMPLETED FOR L5
L6 13 DUP REM L5 (34 DUPLICATES REMOVED)

=> d ibib abs 1-13

L6 ANSWER 1 OF 13 SCISEARCH COPYRIGHT 2003 ISI (R)
ACCESSION NUMBER: 97:55342 SCISEARCH
THE GENUINE ARTICLE: WB018
TITLE: Cloning of human homolog of **Cyr61** and
characterization of its biological activities.
AUTHOR: Kolesnikova T V (Reprint); Lau L F
CORPORATE SOURCE: UNIV ILLINOIS, DEPT GENET, CHICAGO, IL 60607
COUNTRY OF AUTHOR: USA
SOURCE: MOLECULAR BIOLOGY OF THE CELL, (DEC 1996) Vol.
7, Supp. [S], pp. 2412-2412.
Publisher: AMER SOC CELL BIOL, PUBL OFFICE 9650 ROCKVILLE
PIKE, BETHESDA, MD 20814.

ISSN: 1059-1524.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 0

L6 ANSWER 2 OF 13 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 96239486 MEDLINE
DOCUMENT NUMBER: 96239486 PubMed ID: 8657105
TITLE: **Cyr61**, a product of a growth factor-inducible
immediate-early gene, promotes cell proliferation,
migration, and adhesion.
AUTHOR: Kireeva M L; MO F E; Yang G P; Lau L F
CORPORATE SOURCE: Department of Genetics, University of Illinois College of
Medicine, Chicago, 60607-7170, USA.
CONTRACT NUMBER: R01 CA46565-08 (NCI)
SOURCE: MOLECULAR AND CELLULAR BIOLOGY, (1996 Apr) 16 (4)
1326-34.
Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199607
ENTRY DATE: Entered STN: 19960808
Last Updated on STN: 19960808
Entered Medline: 19960729

AB **cyr61** was first identified as a growth factor-inducible
immediate-early gene in mouse fibroblasts. The encoded **Cyr61**
protein is a secreted, cystein-rich heparin-binding protein that
associates with the cell surface and the extracellular matrix, and in
these aspects it resembles the Wnt-1 protein and a number of known growth
factors. During embryogenesis, **cyr61** is expressed most notably
in mesenchymal cells that are differentiating into chondrocytes and in the
vessel walls of the developing circulatory system. **cyr61** is a
member of an emerging gene family that encodes growth regulators,
including the connective tissue growth factor and an avian
proto-oncoprotein, Nov **cyr61** also shares sequence similarities
with two Drosophila genes, twisted gastrulation and short gastrulation,
which interact with decapentaplegic to regulate dorsal-ventral patterning.
In this report we describe the purification of the **Cyr61** protein
in a biologically active form, and we show that purified **Cyr61**
has the following activities: (i) it promotes the attachment and spreading
of endothelial cells in a manner similar to that of fibronectin; (ii) it
enhances the effects of basic fibroblast growth factor and
platelet-derived growth factor on the rate of DNA synthesis of fibroblasts
and vascular endothelial cells, although it has no detectable mitogenic
activity by itself; and (iii) it acts as a chemotactic factor for
fibroblasts. Taken together, these activities indicate that **Cyr61**
is likely to function as an extracellular matrix signaling molecule rather
than as a classical growth factor and may regulate processes of cell
proliferation, migration, adhesion, and differentiation during
development.

L6 ANSWER 3 OF 13 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:96715 BIOSIS
DOCUMENT NUMBER: PREV199799395918
TITLE: Cloning of human homolog of **cyr61** and
characterization of its biological activities.
AUTHOR(S): Kolesnikova, T. V.; Lau, L. F.
CORPORATE SOURCE: Dep. Genet., Univ. Illinois, Chicago, IL 60607 USA
SOURCE: Molecular Biology of the Cell, (1996) Vol. 7, No. SUPPL.,
pp. 415A.
Meeting Info.: Annual Meeting of the 6th International
Congress on Cell Biology and the 36th American Society for

Cell Biology San Francisco, California, USA December 7-11, 1996

ISSN: 1059-1524.

DOCUMENT TYPE: Conference; Abstract; Conference
LANGUAGE: English

L6 ANSWER 4 OF 13 MEDLINE DUPLICATE 2

ACCESSION NUMBER: 96257227 MEDLINE

DOCUMENT NUMBER: 96257227 PubMed ID: 8666280

TITLE: Isolation and characterization of xnov, a *Xenopus laevis* ortholog of the chicken nov gene.

AUTHOR: Ying Z; King M L

CORPORATE SOURCE: Department of Cell Biology and Anatomy, School of Medicine, University of Miami, FL 33101, USA.

CONTRACT NUMBER: GM33932 (NIGMS)

SOURCE: GENE, (1996 Jun 1) 171 (2) 243-8.
Journal code: 7706761. ISSN: 0378-1119.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

OTHER SOURCE: GENBANK-U37063; GENBANK-U37064

ENTRY MONTH: 199608

ENTRY DATE: Entered STN: 19960819

Last Updated on STN: 19980206

Entered Medline: 19960808

AB We have isolated an ortholog (xnov) of the chicken nov gene (for nephroblastoma overexpressed; encoding a putative avian proto-oncogene) from *Xenopus laevis* (Xl) by screening an Xl ovary cDNA library and genomic library using the entire coding region of human CTGF (encoding connective tissue growth factor) as a probe and by 5'RACE (rapid amplification of cDNA ends). xnov has the same genomic organization as chicken nov, mouse fisp12 and **cyr61**, but has a unique promoter sequence. The Xl open reading frame (ORF) encodes a 343-amino-acid (aa) polypeptide of 37.9 kDa. Xnov shows 62.9, 60.5, 52.2, 52.1, 47.6 and 45.8% identity with the chicken Nov, human NovH, human CTGF, mouse Fisp12, chicken Cef10 and mouse **Cyr61** proteins, respectively. Xnov contains four aa domains which characterize the CTGF family. RT-PCR (reverse transcription-polymerase chain reaction) analysis shows that the xnov mRNA is very low in abundance and appears to be present throughout early Xl development. Our results also indicate that xnov and nov are not orthologs of human CTGF.

L6 ANSWER 5 OF 13 MEDLINE DUPLICATE 3

ACCESSION NUMBER: 95348101 MEDLINE

DOCUMENT NUMBER: 95348101 PubMed ID: 7622488

TITLE: Glucocorticoid-attenuated response genes encode intercellular mediators, including a new C-X-C chemokine.

AUTHOR: Smith J B; Herschman H R

CORPORATE SOURCE: Division of Neonatology, UCLA School of Medicine 90095, USA.

CONTRACT NUMBER: GM24797 (NIGMS)

SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1995 Jul 14)
270 (28) 16756-65.

Journal code: 2985121R. ISSN: 0021-9258.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

OTHER SOURCE: GENBANK-U27267

ENTRY MONTH: 199508

ENTRY DATE: Entered STN: 19950911

Last Updated on STN: 19950911

Entered Medline: 19950825

AB A major part of the anti-inflammatory effect of glucocorticoids is attributable to their attenuation of the induction of genes whose products

mediate intercellular interactions, e.g. cytokines and the inducible forms of prostaglandin synthase and nitric oxide synthase. We hypothesized that (i) there exists a class of immediate-early/primary response genes whose induction by inflammatory agents, mitogens, and other stimuli is attenuated by glucocorticoids, and (ii) the products of these glucocorticoid-attenuated response genes (GARGs) function predominantly in paracrine cell processes. We constructed a lambda cDNA library from transforming growth factor beta 1-pretreated murine Swiss 3T3 cells stimulated with lipopolysaccharide (LPS) or serum in the presence of cycloheximide, screened 15,000 plaques by differential hybridization, and cloned 12 LPS-induced, dexamethasone-attenuated cDNAs. Seven were previously known. Six of these encode intercellular mediators (thrombospondin-1, MCSF, JE/MCP-1, MARC/fic/MCP-3, crg2/IP-10, and **cyr61**); one encodes a protein of unknown function (IRG2). Thus, a large majority of these GARG cDNAs encode intercellular mediators, as hypothesized. Of the five GARG cDNAs not previously known, one encodes a novel member of the CXC chemokine family, designated LIX (LPS-induced CXC chemokine). The predicted LIX protein has a 40-amino acid signal sequence and a 92-amino acid mature peptide with a distinctive COOH-terminal region. Surprisingly, segments of the 3'-untranslated regions of LIX and two other CXC chemokines have substantially greater nucleotide sequence homology than do their coding regions. These segments may perform an unknown regulatory function. The LIX message is strongly induced by LPS in fibroblasts, but not in macrophages, suggesting that LIX may participate in the recruitment of inflammatory cells by injured or infected tissue.

L6 ANSWER 6 OF 13 MEDLINE DUPLICATE 4
 ACCESSION NUMBER: 93300535 MEDLINE
 DOCUMENT NUMBER: 93300535 PubMed ID: 8314592
 TITLE: Norrie disease gene: characterization of deletions and possible function.
 AUTHOR: Chen Z Y; Battinelli E M; Hendriks R W; Powell J F; Middleton-Price H; Sims K B; Breakefield X O; Craig I W
 CORPORATE SOURCE: Department of Biochemistry, University of Oxford, United Kingdom.
 SOURCE: GENOMICS, (1993 May) 16 (2) 533-5.
 Journal code: 8800135. ISSN: 0888-7543.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199307
 ENTRY DATE: Entered STN: 19930813
 Last Updated on STN: 19930813
 Entered Medline: 19930726

AB Positional cloning experiments have resulted recently in the isolation of a candidate gene for Norrie disease (pseudoglioma; NDP), a severe X-linked neurodevelopmental disorder. Here we report the isolation and analysis of human genomic DNA clones encompassing the NDP gene. The gene spans 28 kb and consists of 3 exons, the first of which is entirely contained within the 5' untranslated region. Detailed analysis of genomic deletions in Norrie patients shows that they are heterogeneous, both in size and in position. By PCR analysis, we found that expression of the NDP gene was not confined to the eye or to the brain. An extensive DNA and protein sequence comparison between the human NDP gene and related genes from the database revealed homology with cysteine-rich protein-binding domains of immediate-early genes implicated in the regulation of cell proliferation. We propose that NDP is a molecule related in function to these genes and may be involved in a pathway that regulates neural cell differentiation and proliferation.

L6 ANSWER 7 OF 13 MEDLINE DUPLICATE 5
 ACCESSION NUMBER: 93327926 MEDLINE
 DOCUMENT NUMBER: 93327926 PubMed ID: 7687569
 TITLE: The modular architecture of a new family of growth

regulators related to connective tissue growth factor.

AUTHOR: Bork P

CORPORATE SOURCE: Max-Delbrück-Centre for Molecular Medicine, Berlin-Buch, Germany.

SOURCE: FEBS LETTERS, (1993 Jul 26) 327 (2) 125-30. Ref: 42

Journal code: 0155157. ISSN: 0014-5793.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199308

ENTRY DATE: Entered STN: 19930903

Last Updated on STN: 20000810

Entered Medline: 19930824

AB Recently, several groups have characterized and sequenced members of a new family of growth regulators (originally called cef10, connective tissue growth factor, fisp-12, **cyr61**, or, alternatively, beta IG-M1 and beta IG-M2), all of which belong to immediate-early genes expressed after induction by growth factors or certain oncogenes. Sequence analysis of this family revealed the presence of four distinct modules. Each module has homologues in other extracellular mosaic proteins such as Von Willebrand factor, slit, thrombospondins, fibrillar collagens, IGF-binding proteins and mucins. Classification and analysis of these modules suggests the location of binding regions and, by analogy to better characterized modules in other proteins, sheds some light onto the structure of this new family.

L6 ANSWER 8 OF 13 MEDLINE DUPLICATE 6

ACCESSION NUMBER: 93041389 MEDLINE

DOCUMENT NUMBER: 93041389 PubMed ID: 1419914

TITLE: Expression of the growth factor-inducible immediate early gene **cyr61** correlates with chondrogenesis during mouse embryonic development.

AUTHOR: O'Brien T P; Lau L F

CORPORATE SOURCE: Department of Genetics, University of Illinois College of Medicine, Chicago 60612.

CONTRACT NUMBER: CA46565 (NCI)

SOURCE: CELL GROWTH AND DIFFERENTIATION, (1992 Sep) 3 (9) 645-54.

Journal code: 9100024. ISSN: 1044-9523.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199212

ENTRY DATE: Entered STN: 19930122

Last Updated on STN: 19970203

Entered Medline: 19921217

AB **cyr61** is a growth factor-inducible immediate early gene initially identified in serum-stimulated mouse fibroblasts. It encodes a member of an emerging family of cysteine-rich secreted proteins that includes a connective tissue growth factor. We show here that **cyr61** is expressed in the developing mouse embryo and extraembryonic tissues. In the placenta, **cyr61** is expressed in regions of trophoblastic origin, including the ectoplacental cone and the trophoblastic giant cells. In the midgestation embryo, **cyr61** is expressed in the smooth muscle vessel walls of the arterial circulatory system. Most notably, expression is found in developing cartilaginous elements, including the limbs, ribs, and prevertebrae. In addition, regions of the chondrocranium and craniofacial elements, such as Meckel's cartilage, also express **cyr61**. Thus, **cyr61** transcript is found in mesenchymal cells of both mesodermal and ectodermal origin

during their differentiation into chondrocytes. The temporal and spatial regulation of **cyr61** expression and the biochemical features of its encoded protein suggest that **cyr61** may be important for the normal growth, differentiation, or morphogenesis of the cartilaginous skeleton of the embryo.

L6 ANSWER 9 OF 13 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1992:380061 BIOSIS
DOCUMENT NUMBER: BR43:47011
TITLE: THE IMMEDIATE EARLY GENE **CYR61** ENCODES A HEPARIN BINDING PROTEIN WHOSE IN-VIVO EXPRESSION CORRELATES WITH CHONDROGENESIS.
AUTHOR(S): YANG G P; O'BRIEN T P; ABLER A S; LAU L F
CORPORATE SOURCE: DEP. GENET., UNIV. ILL. COLL. MED., CHICAGO, ILL. 60612, USA.
SOURCE: KEYSTONE SYMPOSIUM ON GROWTH AND DIFFERENTIATION FACTORS IN VERTEBRATE DEVELOPMENT, KEYSTONE, COLORADO, USA, APRIL 3-10, 1992. J CELL BIOCHEM SUPPL, (1992) 0 (16 PART F), 104.
CODEN: JCBSD7.
DOCUMENT TYPE: Conference
FILE SEGMENT: BR; OLD
LANGUAGE: English

L6 ANSWER 10 OF 13 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 91288203 MEDLINE
DOCUMENT NUMBER: 91288203 PubMed ID: 2062642
TITLE: Promoter function and structure of the growth factor-inducible immediate early gene **cyr61**.
AUTHOR: Latinkic B V; O'Brien T P; Lau L F
CORPORATE SOURCE: Department of Genetics, University of Illinois College of Medicine, Chicago 60612.
CONTRACT NUMBER: R01 CA52220 (NCI)
SOURCE: NUCLEIC ACIDS RESEARCH, (1991 Jun 25) 19 (12) 3261-7.
Journal code: 0411011. ISSN: 0305-1048.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-X56790; GENBANK-X56865; GENBANK-X57509; GENBANK-X57510; GENBANK-X58491; GENBANK-X58492; GENBANK-X58493; GENBANK-X58494; GENBANK-X58495; GENBANK-X58496
ENTRY MONTH: 199108
ENTRY DATE: Entered STN: 19910825
Last Updated on STN: 19970203
Entered Medline: 19910807

AB **cyr61** is an immediate early gene that is transcriptionally activated in 3T3 fibroblasts by serum, platelet-derived growth factor, fibroblast growth factor, and the tumor promoter TPA with kinetics similar to the induction of c-fos. **cyr61** encodes a secreted protein that is associated with the cell surface and the extracellular matrix, and may play a role in cell-cell communication. We report here the complete nucleotide sequence of the mouse **cyr61** gene, which contains four short introns. The transcription start site was mapped by S1 nuclease and primer extension analyses. A 2 kb 5' flanking DNA fragment functions as a serum-inducible promoter. This DNA fragment contains a poly(CA) sequence that can adopt the Z DNA form. In addition, it contains a sequence that resembles the serum response element (SRE) originally identified in the c-fos promoter. We show that deletion of the **cyr61** SRE-like sequence abrogates serum inducibility. Furthermore, this SRE-like sequence is sufficient to confer serum and growth factor inducibility when linked to a basal promoter, and binds the 67 kD serum response factor in vitro. We conclude that the **cyr61** SRE functions as a serum response

element and may account for the coordinate activation of **cyr61** and c-fos.

L6 ANSWER 11 OF 13 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 92144441 MEDLINE
DOCUMENT NUMBER: 92144441 PubMed ID: 1782153
TITLE: **Cyr61**, product of a growth factor-inducible immediate early gene, is associated with the extracellular matrix and the cell surface.
AUTHOR: Yang G P; Lau L F
CORPORATE SOURCE: Department of Genetics, University of Illinois College of Medicine, Chicago 60612.
CONTRACT NUMBER: RO1 CA46565 (NCI)
SOURCE: CELL GROWTH AND DIFFERENTIATION, (1991 Jul) 2 (7) 351-7.
Journal code: 9100024. ISSN: 1044-9523.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199203
ENTRY DATE: Entered STN: 19920405
Last Updated on STN: 19920405
Entered Medline: 19920313

AB **cyr61** is a specific target for activation by platelet-derived growth factor and fibroblast growth factor and is inducible by the oncogene v-src. It is a member of the class of immediate early genes that includes those encoding protooncogene products, transcription factors, and cytokines. We have previously characterized the synthesis and degradation of the **cyr61**-encoded mRNA and protein. Although the deduced **Cyr61** protein sequence contains an NH2-terminal secretory signal, it is not detectable in the conditioned medium of serum-stimulated cells. We show here that in rapidly growing cell cultures, newly synthesized **Cyr61** is secreted and is associated with both the extracellular matrix and the cell surface. In contrast, **Cyr61** secreted in serum-stimulated quiescent cells is directed to the cell surface and is not incorporated into the extracellular matrix. Once associated with the extracellular matrix, **Cyr61** has a half-life of greater than 24 h, whereas intracellular and cell surface-associated **Cyr61** has an apparent half-life of approximately 30 min. Furthermore, **Cyr61** appears to bind heparin with high affinity. These observations suggest similarities among **Cyr61**, the fibroblast growth factors (heparin-binding growth factors), and the protooncogene product Int-1 and are consistent with the hypothesis that **Cyr61** plays a role in cell-cell communication involving the interaction of neighboring cells.

L6 ANSWER 12 OF 13 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 91229699 MEDLINE
DOCUMENT NUMBER: 91229699 PubMed ID: 2029337
TITLE: Identification of a gene family regulated by transforming growth factor-beta.
AUTHOR: Brunner A; Chinn J; Neubauer M; Purchio A F
CORPORATE SOURCE: Bristol-Myers Squibb Pharmaceutical Research Institute, Seattle, WA 98121.
SOURCE: DNA AND CELL BIOLOGY, (1991 May) 10 (4) 293-300.
Journal code: 9004522. ISSN: 1044-5498.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-M65213; GENBANK-M80263; GENBANK-S60919; GENBANK-S60920; GENBANK-S65647; GENBANK-S65649; GENBANK-X64571; GENBANK-X64572; GENBANK-X64573; GENBANK-X64574
ENTRY MONTH: 199106

ENTRY DATE: Entered STN: 19910707
Last Updated on STN: 19970203
Entered Medline: 19910620

AB We have identified two related genes whose mRNAs are increased after treatment with transforming growth factor-beta (TGF-beta 1). Mouse AKR-2B cells were treated with TGF-beta 1 in the presence of cyclohexamide and a cDNA library was subjected to differential screening. Several TGF-beta-induced genes (beta IG) were isolated and two of these, beta IG-M1 and beta IG-M2, were characterized. beta IG-M1 and beta IG-M2 RNAs were significantly increased after TGF-beta 1 treatment and both were superinduced in the presence of cyclohexamide. cDNA sequence analysis of beta IG-M1 showed that it encoded a 379-amino-acid protein which was 81% homologous to CEF-10, a v-src and TPA-inducible gene, and identical to **cyr61**, a gene induced by serum in growth-arrested BALB-3T3 cells. cDNA sequence analysis of beta IG-M2 showed that it encoded a 348-amino-acid protein that was 50% homologous to beta IG-M1. Thirty-eight cysteine residues are conserved between beta IG-M1 and beta IG-M2, which are clustered at the amino and carboxy ends: The middle regions of the two proteins are cysteine free and display the highest degree of nonhomology. Both proteins contain an amino-terminal cysteine-rich motif common to insulin-like growth factor binding proteins and a carboxy-terminal domain with strong homology to a motif found near the carboxy-terminal of the malarial circumsporozoite protein which may be involved in cell adhesion. The regulation of mRNA encoding these proteins by TGF-beta 1 suggests that they may be involved in mediating some of the pleiotropic effects of this multipotent modulator of cell growth and differentiation.

L6 ANSWER 13 OF 13 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 90287146 MEDLINE
DOCUMENT NUMBER: 90287146 PubMed ID: 2355916
TITLE: Expression of **cyr61**, a growth factor-inducible immediate-early gene.
AUTHOR: O'Brien T P; Yang G P; Sanders L; Lau L F
CORPORATE SOURCE: Department of Genetics, University of Illinois College of Medicine, Chicago 60612.
CONTRACT NUMBER: R01 CA46565 (NCI)
R01 CA52220 (NCI)
SOURCE: MOLECULAR AND CELLULAR BIOLOGY, (1990 Jul) 10 (7) 3569-77.
Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-M32490
ENTRY MONTH: 199007
ENTRY DATE: Entered STN: 19900824
Last Updated on STN: 19900824
Entered Medline: 19900720

AB A set of immediate-early genes that are rapidly activated by serum or purified platelet-derived growth factor in mouse 3T3 fibroblasts has been previously identified. Among these genes, several are related to known or putative transcription factors and growth factors, supporting the notion that some of these genes encode regulatory molecules important to cell growth. We show here that a member of this set of genes, **cyr61** (originally identified by its cDNA 3CH61), encodes a 379-amino-acid polypeptide rich in cysteine residues. **cyr61** can be induced through protein kinase C-dependent and -independent pathways. Unlike many immediate-early genes that are transiently expressed, the **cyr61** mRNA is accumulated from the G0/G1 transition through mid-G1. This expression pattern is due to persistent transcription, while the mRNA is rapidly turned over during the G0/G1 transition and in mid-G1 at the same rate. In logarithmically growing cells, the **cyr61** mRNA level is constant throughout the cell cycle. **Cyr61** contains an N-terminal secretory signal sequence; however, it is not detected in the culture

medium by immunoprecipitation. **Cyr61** is synthesized maximally at 1 to 2 h after serum stimulation and has a short half-life within the cell.

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---Logging off of STN---

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Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	20.84	26.93

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